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10/585,651	07/07/2006	Philip C. Trackman	BU-112XX	5481

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EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	PAPER NUMBER
1652	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,651	TRACKMAN ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *8-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election with traverse of group I (claims 1-7) in their response of 09/22/2008 is acknowledged. The traversal is on the ground(s) that there was no lack of unity with regard to the pending claims and there should not be an undue burden of search to consider all the groups. Applicant's arguments have been fully considered, but they are found unpersuasive. Claims are not linked by a special technical feature, as explained in the previous office. Further evidence that the claims lack special technical feature is found in rejection below under U.S.C.102. Therefore, the restriction remains proper and the restriction made FINAL.

Specification Objection

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code at page 6 lines 9 and 12. See MPEP § 608.01.

Sequence compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. For example see the specification at page 22 lines 20 and 21. Appropriate correction is required. See particularly 37 CFR 1.821(d).

Priority

This application is a 371 of PCT/US05/00631, filed 01/06/2005, which claims priority to US provisional application 60/536109, filed 01/1392004.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 01/11/2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the IDS statement.

Objection

Figures 3A-3D are objected because it contains amino acid sequence designated by low key letter. It is the convention in the art to write amino acid sequences with a single capital letter. Appropriate corrections are required

Claim Rejection

35 U.S.C 112 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 , 4-5 (dependent on claim 1) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 4-5 (dependent on claim 1) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in recitation the phrase "a therapeutically active portion" because it is unclear what a therapeutically active portion constitute and what is the therapeutically activity.

35 U.S.C 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5 directed to therapeutic composition comprising active portion of any lysyl oxidase pro-peptide lacking enzymatic activity from any source having any structure (claims 1-3) or any lysyl oxidase pro-peptide variant (claims 4-5) wherein said variant comprise any lysyl oxidase pro-peptide having any number of conservative substitutions of SEQ ID NO: 1-8. The specification teaches the structure of only a few representative species of such therapeutic composition comprising active portion of pro-peptide lacking enzymatic activity comprising human lysyl oxidase SEQ ID NOs: 1, 3 and 6; mouse lysyl oxidase comprising SEQ ID NOs: 2, 4 and 7 and rat lysyl oxidase of SEQ ID NOs: 5 and 8. The SEQ ID NOs: 1 and 2 are full length lysyl oxidase and SEQ ID NO: 3-8 are pro-polypeptide variants comprising 35-37 amino acids. The specification fails to describe any other representative species by any identifying characteristics or properties other than the biological activity lacking enzymatic activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full,

clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

In University of California v. Eli Lilly & Co., 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case the scope of the instant claims encompass any lysyl oxidase pro-peptide lacking enzymatic activity from any source or any variant comprising any number of conservative substitutions of SEQ ID NOs: 1-8 lysyl oxidase enzymatic

activity. Thus, the claimed therapeutic composition comprises a polypeptide **having any structure**. WO/0185157, a qualified prior art, teach active portion of lysyl oxidase and its homolog with or without catalytic activity and specification teaches (page 3) some propolypeptides (SEQ ID NOs: 1-8). The specification fails to describe any other representative species by sufficient identifying characteristics or properties to show that applicant was in possession of the claimed genus.

There is no structure-function correlation with regard to the members of the genus of therapeutic composition comprising active portion of any lysyl oxidase pro-peptide lacking enzymatic activity and structural details and any active portion of any lysyl oxidase pro-peptide comprising any fragments of SEQ ID NOs: 1-8 having one or more mutation(s) comprise any structure claimed in the instant claims. Therefore one of skill in the art would not recognize from the disclosure that applicants' were in possession of the claimed inventions. Applicants' are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for therapeutic composition comprising active portion of any human lysyl oxidase pro-peptide lacking enzymatic activity or lysyl oxidase comprising SEQ ID NOs:1-8, and method of identifying active portion of lysyl oxidase pro-polypeptide using a fragments of SEQ ID NO:3-8, does not reasonably provide enablement for any therapeutic composition comprising active portion of any lysyl

oxidase pro-peptide lacking enzymatic activity from any source having any structure (claims 1-3) or any fragments of non-human lysyl oxidase comprising SEQ ID NOs: 2, 4-5 and 7-8 having any conservative substitutions thereof (claims 4-5) and method of identifying any active portion of lysyl oxidase pro-polypeptide using any fragment of any lysyl oxidase propolypeptide (claims 6-7). The therapeutic compositions comprising active portion of pro-peptide lacking enzymatic activity comprise human lysyl oxidase of SEQ ID NOs: 1, 3 and 6; mouse lysyl oxidase comprising SEQ ID NOs: 2, 4 and 7 and rat lysyl oxidase of SEQ ID NOs: 5 and 8. The SEQ ID NOs: 1 and 2 are full length lysyl oxidase and SEQ ID NO: 3-8 are pro-polypeptide variants comprising 35-37 amino acids. These sequences comprise varied polypeptide having diverse structure. Specification teach that pro-peptide region of lysyl oxidase less well conserved in some region and well conserved in other region of the sequences of different species(page 8, line 5-20). Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

According to MPEP 2164.01(a), factors considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G)

The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

MPEP§ 2164.04 states that while the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. Accordingly, the factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claims 1-3, 6-7 are directed to include therapeutic composition comprising active portion of any lysyl oxidase pro-peptide lacking enzymatic activity from any source having any structure (claims 1-3) or method of identifying any active portion of lysyl oxidase pro-polypeptide using any fragment of any lysyl oxidase propolypeptide (claims 6-7).

The state of the prior art; The relative skill of those in the art; and The predictability or unpredictability of the art: The state of the art regarding include therapeutic composition comprising active portion of lysyl oxidase pro-peptide lacking enzymatic activity is limited to 50 kDa propolypeptide. However, the instant claims 1-3 are encompass any lysyl oxidase pro-peptide lacking enzymatic activity from any source having any structure.

The positions within a protein's amino acid sequence where modifications can be made with a reasonable expectation of success in obtaining a lysyl oxidase pro-peptide lacking enzymatic activity leading to biological activity are limited in any protein's structure and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g., multiple substitutions, deletions, additions, and combinations thereof.

Methods for isolating or generating variants and mutants using random mutagenesis techniques were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the amino acid sequence of any lysyl oxidase from any source to obtain a biologically active and lacking enzymatic active propolypeptide. At the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the same desired biological activity

The amino acid sequence of a protein determines the structural and functional properties of that protein. In the instant case, neither the specification nor the art provide a correlation between structure and activity such that one of skill in the art can envision the structure of any of the propolypeptide recited in the claims 1, 4 have desired biological activity. It is well known in the prior art that the amino acid sequence of a protein determines the protein's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence to obtain a desired biological activity, requires knowledge and guidance regarding specific amino acid

residue(s) in the protein's amino acid sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification) and detailed knowledge of the protein's structure, and the ways in which the protein's structure relates to its function. The reference of Chica et al. (Curr Opin Biotechnol. 2005 Aug; 16(4):378-84) teaches that the complexity of the structure/function relationship in enzymes has proven to be the factor limiting the general application of rational enzyme modification and design, where rational enzyme modification and design requires in-depth understanding of structure/function relationships.

The amount of direction provided by the inventor; and the existence of working examples: Claims 1-3, 6--7 are directed to include therapeutic composition comprising active portion of any lysyl oxidase pro-peptide lacking enzymatic activity from any source having any structure (claims 1-3) method of identifying any active portion of lysyl oxidase pro-polypeptide using any fragment of any lysyl oxidase propolypeptide. However, the specification fails to disclose any specific guidance for obtaining a propolypeptide from any lysyl oxidase from any source such that said propolypeptide shows biological activity and lack enzymatic activity or mutating specific conserve amino acid residues of SEQ ID NO: 1-2 to obtain a biologically active and enzymatically inactive protein, because guidance and working examples teaching unalterable structural and catalytic amino acid residues and amino acid residues tolerable to change is not provided by the specification.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating and/or generating variants of a

polypeptide were known in the art at the time of the invention and the specification provides general teachings for searching and screening for the claimed invention, it was not routine in the art to screen by a trial and error process for all polypeptides having a substantial number of modifications as encompassed by the claim(s) for those that maintain the same desired biological activity and lack enzymatic activity. General teachings from the specification regarding screening and searching for the claimed invention using biological and enzyme assays is not specific guidance for making and using the claimed invention.

Therefore, in view of the specification's lack of specific guidance and additional working examples, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, it would require undue experimentation for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988).

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (WO/0185157, November 15, 2001). Li et al teach lysyl oxidase polypeptide inhibits the cancer cell growths on agar plate (pages 41, lines 25-33, page 42, lines 1-30) wherein said polypeptide or its homolog may or may not have catalytic activity (page 10 lines 25-33, and page 13, lines 25-28).

Allowable Subject Matter/Conclusion

Claims 1-7 are rejected and none of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NASHAAT T NASHED can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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